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Telegrams
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LONDON, W.12

25 January, 1953.

My dear Lederberg,

I really do feel I owe you an apology for not having written for so long. I am rather a lazy person at root and have a lot of inertia to overcome before embarking on a long letter. Moreover I have been very busy getting nowhere (or, perhaps, not knowing where I'm getting would express it better) and had little new to tell you. First of all, many thanks for the reprints. I had intended writing to you for them and had actually half completed a very long letter to you several weeks ago which is still "shelved" on my desk. I have succeeded in more or less convincing myself that the only fertile cross, so far as individual cells are concerned is F+ X F- (including F- phenocopy). My evidence for this as follows. If the limited fertility of F+ X F+ crosses is due to the development of cells which behave as F- within F+ clones then the fertility of these F- cells should be destroyed by SM-treatment; i.e. if F+ cells cannot mate together, then in AF+sm^t X BF+, AF+sm^t should behave as pure F+ and BF+ as pure F- as judged by prototroph analysis. This is in fact the case, analysis of prototrophs from AF+sm^t X BF+ showing the same distribution as in AF+ X BF-, and from AF+ X BF+sm^t the same distribution as in AF- X BF+. The cross AF+sm^t X BF+sm^t is sterile. When taken in conjunction with the polarising effect of UV. in F+ X F+ crosses I think this evidence is convincing. I also have some evidence that F+ is pathogenic. F- strains transduced to F+ tend to die out under storage conditions which preserve F- strains indefinitely. Moreover, F+ strains reach a significantly lower final population density than homologous F- strains when grown in appropriately supplemented synthetic medium. I do not know whether this is due to lysis or to a decreased generation time. I have also some evidence (though I would not stand by this, as yet) that if, in an M-F+ X TLB$_1$-F- cross, the F+ parent is kept in buffered saline for 1½-2 hours before mixing with the F- parent instead of mixing at once, there is a significantly lower number of Lac and Az cross-overs: as if standing in saline had the effect of whittling down the F+ chromosomal contribution to the bare TL selected markers. This I am confirming (or otherwise) and must repeat in terms of pH, DN-ase &c. My last piece of K-12 news is that I have recently isolated an Hfr strain arising <u>spontaneously</u> in 58-161(Spicer)F- transduced to F+. I have not yet completed investigation of this strain which, unfortunately, is S^{r}Az^r. Would you like it? I nearly forgot to tell you (you probably already know) that only 30% prototrophs are F+ in the 58-161(Spicer)F- X W677/F+ cross. I think this is due to instability of F+ in 58(Spicer) and not to segregation. I have some genetic evidence for this, apart from the fact that 58(Spicer) has a much lower efficiency of transduction to F+ than has W677. On the other hand, 100% prototrophs

from a mating of W677/F+ with an F- phenocopy of 58(Spicer)F+ are F+.

You will already know that I have been invited to the CSH Symposium in June. I have not yet decided just what line to take. In the absence, as yet, of any precise information about the nature or function of F+ which might have clearcut application to virus work, I expect I shall have to be just empirical and provocative, so I hope you will not be too unkind in your discussion! I am looking forward to meeting you and you wife. I see quite a lot of Bruce Stocker who is a great admirer of yours. He seems to have enjoyed the time he spent with you and is at present much engaged with Salmonella transduction. Incidentally, I may be writing to you again, when I get down to writing a draft of this CSH thing, to ask you for confirmation of, and permission to quote, some of your lambda and transduction findings of which I have only hear-say evidence - particularly about the transmission of Gal4 and the fact that in S.typhimurium transduction it is possible for the transduced strain to remain phage sensitive. I still think it probable that F+ will turn out to be a genetic vector. If, for argument's sake, you accept the premises that only F+ & F- cells can mate and that part of the genetic content of the F+ parent is transferred to the F- parent, it is difficult otherwise to explain the determining role of the F+ agent in the process. Or is it? I do'nt know!

With kindest regards and best wishes.

Bill Hayes

Don't bother to reply as yet, as I'm sure you are very busy.

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